UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/365,241	07/30/1999	THOMAS BRODIN	003300-581	1539

21839 7590 09/24/2003

BURNS DOANE SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
PONNALURI, PADMASHRI	

ART UNIT	PAPER NUMBER
1639	34

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/365,241	Brodin et al
Examiner	**Art Unit**
Padmashri Ponnaluri	1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 25, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *66-99* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *66-99* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☒ Interview Summary (PTO-413) Paper No(s). *34*
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The amendment G filed on 6/25/03 has been fully considered and entered into the application.

2. New claim 99 has been added by the amendment G, filed on 6/25/03. Applicants cancel claim 65 which was added by the amendment filed on 11/19/01, and corrects the numbering of claims 65-97 as claims 66-98 by the amendment G, filed on 6/25/03.

3. Claims 66-99 are currently pending and are being examined in this application.

4. The formal drawings filed on 6/25/03 have been fully considered and entered into the application.

5. The previous office action inadvertently mis-numbed the claims as 65-64(pending and rejected), which should read as claims 65-97. Examiner apologizes for any inconvenience caused by the mis-numbering of the claims.

6. Rejections (D, E) of claims 65-94 (renumbered claims 66-95) (rejections of claim 65 in page 5 and 6 of the previous office action mailed on 3/25/03) under 35 U. S. C. 112, second paragraph have been maintained for the reasons of record.

7. Rejections of claim 65 (renumbered as 66), as indefinite by reciting 'scFv/Fab fragment thereof'; 'target structure'; and rejections of claims 69, 91-93 and 95 have been withdrawn in view of the amendments to the claim.

8. The rejections of claims 88-91 (renumbered) under 35 U. S. C. . 112, first paragraph set forth in the previous office action mailed on 3/25/03 have been maintained for the reasons of record.

9. The rejection of claims 65-76, 78-80, 84-86, 91 (the newly renumbered calims 66-77, 79-81, 85-87, 92 and 99) under 35 U. S. C. . 102 (b), set forth in the previous office action mailed on 3/25/03 have been maintained for the reasons of record.

Response to Arguments

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. Applicant's arguments regarding the rejection (D) of claim 65 (renumbered 66) filed on 6/25/03 have been fully considered but they are not persuasive.

D) The instant claimed method is vague and indefinite, according to the instant claimed method of acquiring a monoclonal antibody to a target comprises:

a) exposing a first mounted tissue to an antibody library;

b) eluting the unbound elements to the first mounted tissue(first enriched library);

c) recovering the bound elements to the first mounted tissue (second enriched library) and the monoclonal antibody remains bound to the first mounted tissue (interpreted as that an antibody from the library is left uncleaved to the mounted tissue);

d) amplifying first and second enriched libraries;

e) repeating steps A) to B) to negatively enrich or repeating steps A) to C) to positively enrich;

f) exposing the positively and negatively enriched to a second mounted tissue;

g) eluting the unbound elements to the second mounted tissue(third enriched library);

h) recovering the bound elements to the mounted tissue (fourth enriched library) and the monoclonal antibody remains bound to the second mounted tissue (interpreted as that an antibody from the library is left uncleaved to the mounted tissue);

I) isolating an individual element from either the third or fourth enriched libraries, wherein the individual element is the monoclonal antibodies.

The claimed method seem to be having several problems. Initially in step c) recites that the monoclonal antibody remains unbound to the first mounted tissue. Thus the monoclonal antibody to the target is acquired. Does applicants mean that the bound elements comprise the monoclonal antibody to the target and the bound elements are cleaved from the mounted tissue.

Applicants have amended claim 66 to clarify the issues. However, the amended and renumbered claim 66 is vague and indefinite. According to the method step B) recites 'recovering second enriched library comprising bound elements from a target structure in first mounted tissue, ***such that a monoclonal antibody or scFv/Fab antibody fragment remains bound to the first mounted tissue..'*** *According to the step B) of the instant method, second enriched library comprising cleaved bound elements, it is not clear what does applicants mean by 'such that monoclonal antibody remains bound to the first mounted tissue. Does applicants mean that the second enriched library comprising bound elements has monoclonal antibody, or the monoclonal antibody remain bound to the first mounted tissue even after forming the second enriched library.*

To clarify the confusion applicants may amend the claim by deleting 'such that a monoclonal antibody or scFv/Fab antibody fragment remains bound to the first mounted tissue..'

12. Applicant's arguments regarding the rejection (E) of claim 65 (renumbered 66) filed on 6/25/03 have been fully considered but they are not persuasive.

E) Further it is unclear according to the last step I) how a monoclonal antibody to the target is isolated or identified from the third enriched library which contains only unbound elements to both the first mounted tissue and second mounted tissue. Applicants are requested to amend the claim such that the method steps are clear.

Applicants argue that the first enriched library contains mostly unbound elements to the first tissue, second enriched library contains bound elements to the first tissue, and ***the third enriched library contains mostly elements that bind to the first mounted tissue, but not the second mounted tissue*** *(see applicants response page 17). This seems to be contrary to the instant claimed method. According to the instant method, step D) recites exposing the first (unbound to the first tissue) or second enriched library (bound to the first tissue) to a second mounted tissue..., and step E) recites that eluting from the* ***second mounted tissue unbound elements, wherein the unbound elements comprise a third enriched library****....' Thus according to the instant claimed method steps, the third enriched library may have both the the first enriched library members and the second enriched library members, not the just second mounted tissue as in the applicants arguments.*

*Applicants further argue that 'the fourth enriched library contains mostly elements that do not bind to the first mounted tissue bu do bind to the second mounted tissue. However, The instant method recites '****recovering fourth enriched library comprising elements bound to the second mounted tissue..'*** *which is interpreted as the fourth enriched library may have both the*

first enriched library members and the second enriched library members' not just the first enriched library members as in applicants arguments.

Applicants response does not address the method step (G), 'isolating an individual element from either the third or fourth enriched libraries, wherein the individual element is monoclonal antibody..' According to applicants arguments that third enriched library contains elements that bind to the first mounted tissue (second enriched library), but do not second mounted tissue; and the fourth enriched library contains mostly elements that do not bind to the first mounted tissue (first enriched library) but do bind to the second mounted tissue. Does applicants mean that the monoclonal antibody of interest binds to ***either the first mounted tissue or second mounted tissue*** *Or the he monoclonal antibody of applicants interest* ***binds to both first mounted tissue and second mounted tissue.***

It still is not clear exactly which elements applicants are referring to monoclonal antibody. *Because in step B) the second enriched library has monoclonal antibodies, and in step E) fourth enriched library has monoclonal antibody. And how does the third enriched library has monoclonal antibody it is not clear, because in step E), second paragraph recites that the 'monoclonal antibody ... remains bound to the second mounted tissue...'*

13. Applicant's arguments regarding the 112, first paragraph rejection of record have been fully considered but they are not persuasive.

The instant claims briefly recite that the initial antibody library further comprises antibody identifying information.

The specification discloses methods for acquiring a monoclonal antibody to a target by screening an antibody library with mounted tissue. However, the specification does not disclose any initial library comprising amino acid sequence or nucleic acid sequence which identifies an antibody, which would not meet the written description provision of 35 U.S.C 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, the initial antibody library comprising sequence identifying information as claimed in claims 87-90 do not meet the written description provision of 35 U.S.C 112, first paragraph.

Applicants argue that the present specification does provide written description support for this terminology. Applicants argue that the specification page 7, describes genetic and/or other antibody-identifying information. Further applicants refer to the phage display library, wherein the nucleic acid encoding the antibody is the antibody-identifying information. And further applicants argue that the antibody or antibody fragment are 'labeled' such that the antibody can be reproduced once it is isolated in the claimed method.

Applicants arguments have been considered and are not persuasive, because the specification does not disclose 'a label' or 'tag' in the specification. If applicants mean that the sequence (amino acid or nucleic acid) of the identified antibody is determined, applicants are requested to amend the claim to clearly recite the method steps.

Applicants in the response in page 20 last paragraph state that the 'the examples of the present specification clearly disclose the use of phage cDNA to determine and reproduce the structure of the molecule...' which is clearly not the support for the claimed invention (sequence identifying information). Further applicants argue that page 7 of the specification describe polysome or coded beads, which would refer to a tag, not a nucleic acid as sequence identifying information (i.e., nucleic acid tag). Thus for the reasons set fourth in the previous office action the rejection has been maintained.

14. Applicant's arguments filed on 6/25/03, regarding the art rejection of record have been fully considered but they are not persuasive.

Cai et al teach a melanoma specific VH antibody cloned from a fusion phage library of a vaccinated melanoma patient. The reference teaches human antimelanoma antibody V86 cloned form a single chain Fv molecule fusion phage library (refers to initial antibody library of the instant claims) (refers to instant claims 84-85) displaying the heavy chain variable domain and light chain variable domain of a mealnoma patient. The reference teaches that tissue sections cut from the frozen tissue cells of melanoma tumors or normal skin (refers to mounted tissue of the instant claims 80) and are used for immunohistochemistry which followed the method steps of cultured cells. That is the frozen tissue exposed to the V86 phage library. The unbound phage washed, and the bound phage was identified.

The reference teaches the Panning method of V86 library (refers to instant claims 66-68). The melanoma cell line (refers to instant claim 75-76) was added to the V86 library, and the unbound phage was removed (refers to step b) of the instant claims). The bound phage was eluted from the cells (refers to step c) of the instant claims). The reference teaches that the eluted phage are amplified (refers to the instant claim step d), and claim 86. The reference teaches that for each subsequent panning step, the amplified phage from the previous panning step were used for panning against mealnoma A2058 cells (refers to steps f-I) of the instant claims).

The reference teaches that the relative binding affinities of the fusion phage antibodies to melanoma cells (refers to the instant claim 69). The reference in figure 1, shows that the immunohistochemical staining of mealnoma DM414 cells with V86 library (panel a); and panel b shows the immunohistochemical staining of melanoma A2058 cells with V86 library. The reference teaches that the melanoma specific binding of V86 was further tested by immunohistochemistry with several of the tumor cell lines ans normal cells. The reference teaches that eh V86 can bind specifically to melanoma cells in a metastatic tumor as well as to cultured melanoma cells in metastatic tumor as well as to cultured melanoma cells (refers to instant claims 70-71 of the instant claims). The reference clearly anticipates the claimed invention.

Applicants argue that Cai et al use melanoma cell lines for panning. And the reference further use the both the cell line and tissue sections for performing the immunohistochemistry to confirm the specificity of the V86 antibody identified during the panning method.

Applicants further argue that Cai et al describe panning of the light chains of and the characterization of antibody V86 that was previously identified in a panning procedure using immortalized cell lines. Applicants arguments have been considered and are not persuasive, since Cai et al does screen the V86 antibody library using two different melanoma cells (DM414, and A2058) (immunohistochemical staining refers to 'mounted tissue' of the instant

claims). Applicants argue that Cai et al panning method is directed only towards screening of the V86 antibodies and the method of presently claimed invention is fundamentally different from that described in either Cai et al.

Applicants argue that Cai et al can only disclose the detection of antibodies to external cell antigens, in contrast, ***the presently claimed invention possesses the ability to isolate in the tissue sections. The approach of the present claimed invention exposes the entire cell antigen portfolio.*** *Applicants arguments have been considered and are not persuasive, because the features upon which applicant relies (i.e., tissue sections) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).*

Further applicants argue that Cai et al absorb only once against normal tissue to remove those phage reactive against normal cell surface antigens, while the presently claimed invention permits the alternating use of normal and altered tissue to greatly enhance the detection of rare phage.. Applicants arguments are not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the alternating use of normal and altered tissue) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants argue that Cai et al do not teach the use of differential use of mounted tissue sections to enhance the detection of specific targets as claimed. Applicants arguments are not persuasive, since Cai et al teach the use of normal cells and melanoma cells which would refer to the differential use of tissue.

Applicants argue that there is a significant difference between using cell line cultures for panning versus primary tissue. First a cell line is not a reiteration as the tumor itself in every sense, so antigens expressed on the surface of a cell line will be very different to those in the primary tumor. Applicants arguments have been considered and are not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., tumor tissue) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants arguments regarding the technical difficulties that need to overcome in the order to use tissue sections have been considered and are not persuasive for the reasons discussed supra.

The rejections of record have been maintained for the reasons of record.

Conclusion

15. No claims are allowed.

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner is on ***Increased Flex Schedule*** and can normally be reached on Monday to Friday from 7.00 AM to 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

P. Ponnaluri
Primary Examiner
Technology Center 1600
Art Unit 1639
22 September 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER